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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/811,123	ERICKSON ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6,8-21 and 24-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2, 4-6, 8-21 and 24-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment received June 18, 2004 is acknowledged. Claims 1, 4-6, 14, 15, 26, 28, and 31 were amended. Clams 22 and 23 were canceled.

Claims 1, 2, 4-6, 8-21, and 24-48 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

3. The rejection of claim 26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment to claim 26, limiting R to "SH".

4. The rejection of claims 1, 4-6, and 8-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

Claim Rejections Maintained:

5. The rejection of claims 1, 2, 4, 5, 8-12, 14-17, 20, 24-33, and 38-41 under 35 U.S.C. 103(a) as being unpatentable over Chari (U.S. Patent 5,208,020; issued May 4, 1993; effective filing date Oct. 25, 1989) in view of Hudziak (U.S. Patent 5,725,856; issued Mar. 10, 1998;

effective filing date Jan. 12, 1988) and further in view of Lewis (Lewis, G.D. et al, Cancer Immunol. Immunother. 37: 255-263, 1993; cited in the IDS) is maintained for the reasons of record.

6. The rejection of claims 1, 2, 4, 5, 8-20, 24-33, 38-41 and 46-48 under 35 U.S.C. 103(a) as being unpatentable over Chari (U.S. Patent 5,208,020; issued May 4, 1993; effective filing date Oct. 25, 1989) in view of Carter (U.S. Patent 6,054,297; issued Apr. 25, 2000; effective filing date Aug. 21, 1992) and further in view of Lewis (Lewis, G.D. et al, Cancer Immunol. Immunother. 37: 255-263, 1993; cited in the IDS) is maintained for the reasons of record.

7. The rejection of claims 1, 2, 4-6, 8-12, 14, 20, 24-33 and 38-41 under 35 U.S.C. 103(a) as being unpatentable over Chari (U.S. Patent 5,208,020; issued May 4, 1993; effective filing date Oct. 25, 1989) in view of Bacus (U.S. Patent 5,514,554; issued May 7, 1996; filing date Oct. 7, 1993) and further in view of Lewis (Lewis, G.D. et al, Cancer Immunol. Immunother. 37: 255-263, 1993; cited in the IDS) is maintained for the reasons of record.

8. The rejection of claims 1, 2, 8-14, and 20, 24-33 under 35 U.S.C. 103(a) as being unpatentable over Chari (U.S. Patent 5,208,020; issued May 4, 1993; effective filing date Oct. 25, 1989) in view of Huston (U.S. Patent 5,877,305; issued Mar. 2, 1999; effective filing date Feb. 6, 1992) and further in view of Lewis (Lewis, G.D. et al, Cancer Immunol. Immunother. 37: 255-263, 1993; cited in the IDS) is maintained for the reasons of record.

9. The rejection of claims 1, 2, 8-12, 24-33 and 38-41 under 35 U.S.C. 103(a) as being unpatentable over Chari (U.S. Patent 5,208,020; issued May 4, 1993; effective filing date Oct. 25, 1989) in view of King (U.S. Patent 5,747,261; issued May. 5, 1998; effective filing date Mar. 5, 1986) and further in view of Lewis (Lewis, G.D. et al, Cancer Immunol. Immunother. 37: 255-263, 1993; cited in the IDS) is maintained for the reasons of record.

10. The rejection of claims 1, 34, 44 and 45 under 35 U.S.C. 103(a) as being unpatentable over Chari (supra) in combination with Hudziak (supra), Baccus (supra), Huston (supra) or King (supra), in view of Lewis (supra) as applied to claim 1 above, and further in view of Senger (U.S. Patent 6,022,541; issued 2/8/2000; effective filing 3/3/1997) is maintained for the reasons of record.

11. The rejection of claims 1, 34-37, 42 and 43 under 35 U.S.C. 103(a) as being unpatentable over Chari (supra) in combination with Hudziak (supra), Baccus (supra), Huston (supra) or King (supra), in view of Lewis (supra) as applied to claim 1 above, and further in view of Sliwkowski (Sliwkowski, M.X. et al., J. Biol.Chem. 269: 14661-14665, 1994; IDS) or Carter (supra) is maintained for the reasons of record.

12. The rejection of claims 1, 4-6, 8-19, 22-25, 27 and 32 under 35 U.S.C. 103(a) as being unpatentable over Iwassa (U.S. Patent 5,217,713; issued Jun. 8, 1993; effective filing date Dec. 27, 1989) in combination with Carter (supra), Hudziak (supra), Baccus (supra), Huston (supra) or King (supra), in view of Lewis (supra) is maintained for the reasons of record.

Response to Arguments

13. The rejections maintained above in items #5 through #9 are treated together for the purposes of answering applicants' arguments because the arguments are essentially the same for each of these rejections. Applicants argue that the cited references fail to provide any suggestion or motivation to combine, and also the cited references fail to provide a reasonable expectation of success. These arguments are not found persuasive. The motivation to combine the teachings of the references is derived from the teachings of Chari that maytansinoids may be linked to a monoclonal antibody or fragment for the purpose of selectively delivering maytansinoids to a selected cell population. Chari clearly contemplates using monoclonal antibodies that are selective for tumor cell antigens. Each of Carter, Hudziak, Baccus, Huston, or King teaches antibodies that bind to a tumor antigen, ErbB2, and teaches that these antibodies are useful in methods of targeting toxins to tumor cells. Because each of Carter, Hudziak, Baccus, Huston, or King teaches the use of their anti-ErbB2 antibodies as antibodies that would act as carriers to selectively deliver a toxin to tumor cells, the motivation to combine the references is that Chari teaches the desirability of increasing the selectivity of maytansinoid constructs and any of Carter, Hudziak, Baccus, Huston, or King teaches that anti-ErbB2 antibodies are useful as carriers to increase the selectivity of toxins.

Applicant has also argued that one of ordinary skill in the art would not have had a reasonable expectation of success in treating a tumor with an anti-ErbB2 antibody-maytansinoid conjugate, where the tumor is one that does not respond, or responds poorly to treatment with an anti-ErbB2 antibody. As a preliminary matter, it is noted that the claims are not limited to methods comprising administering a maytansinoid conjugate to a mammal having a tumor that

does not respond, or responds poorly to an anti-ErbB2 antibody. The methods, as currently recited, comprise administering a maytansinoid conjugate to a mammal having a tumor. The fact that claimed methods comprise two preceding steps comprising determining different aspects of the tumor does not change the scope of the third administration step as it is currently recited. However, the scope of the claims not-withstanding, the claims encompass treating mammals having tumors that over-express ErbB2 and also do not respond or respond poorly to treatment with an anti-ErbB2 antibody, and such methods are obvious over the prior art because it is known to use antibodies to ErbB2 as carriers for toxins for the purpose of increasing the selectivity of the toxin. Therefore, the ability of the anti-ErbB2 antibody induce a growth effect or cytoxic effect is irrelevant, because the anti-ErbB2 antibody is conjugated to a toxic compound, a maytansinoid. Because it is known that maytansinoids can be linked to antibodies to increase their selectivity, and that an increase in the selectivity of maytansinoids is desirable because unconjugated maytansinoids are highly cytotoxic and produce side-effects in vivo (U.S. Patent 5,208,020; col. 3, lines 45-58), the motivation to make anti-ErbB2 antibody-maytansinoid conjugates is present in the teachings of the cited references.

Additionally, applicant appears to be arguing that there is no expectation of success for a method of treating a population of patients having a tumor that does not respond, or responds poorly to an anti-ErbB2 antibody. It appears that applicant is arguing that if a tumor does not respond to treatment with an unconjugated anti-ErbB2 antibody, then it would be surprising to discover that the same tumor will respond to a maytansinoid. This argument is not found persuasive, because neither the specification nor the prior art suggests that a tumor failing to respond to treatment with an unconjugated anti-ErbB2 antibody is a tumor that is resistant to any

other treatment, or specifically resistant to maytansinoids. Additionally, Chari teaches that maytansinoids are highly cytotoxic. Applicant has not provided evidence for why failure with one mode of treatment would lead one to the expectation of failure in a second, very different, mode of treatment. Regardless, as discussed above, the scope of the methods encompasses treating all tumors. Therefore, the expectation of success is derived from the teachings that anti-ErbB2 antibodies may be used as carrier for toxins and that maytansinoids are highly toxic compounds.

However, even if the claims were amended to change the scope of the administration step, methods for treating patients having tumors that do not respond or respond poorly to treatment with an anti-ErbB2 antibody would be obvious over the prior art, because tumors that do not respond to anti-ErbB2 antibodies are known to exist (teachings of Lewis) and because the growth inhibitory properties of the carrier antibody do not appear to be relevant in a method comprising the use of a maytansinoid conjugate where the cytotoxicity of the maytansinoid conjugate is used to treat the tumor.

14. Applicants argue that the rejection maintained above in item #10 should be withdrawn because there is no link between the methods of Senger and the claimed methods. This is not found persuasive. The rejection over Chari in combination with Hudziak (supra), Baccus (supra), Huston (supra) or King (supra), in view of Lewis (supra) as applied to claim 1 above, and further in view of Senger was made to address one embodiment of the claimed methods where two antibodies conjugated to toxins are used. Senger teaches such a strategy and exemplifies his method by using antibodies that bind to VPF. The claimed methods, when they

are construed as methods comprising the use of two antibodies conjugated to toxins, differ from the teachings of Chari in combination with Hudziak (supra), Baccus (supra), Huston (supra) or King (supra), because Chari teaches the use of one antibody. However, the strategy of using more than one antibody is known in the art as evidenced by the teachings of Senger. Therefore, the teachings of Senger demonstrate that the strategy of using more than one antibody-toxin conjugate is already known in the art and the limitations of claims 34, 44 or 45 do not render the claims unobvious over the prior art that has already been applied to claim 1.

15. Applicants argue that the rejection maintained above in item #11 should be withdrawn because it is not understood how the rejection may be made in light of In re Kerkoven. The rejection of claims 1, 34-37, 42 and 43 under 35 U.S.C. 103(a) as being unpatentable over Chari (supra) in combination with Hudziak (supra), Baccus (supra), Huston (supra) or King (supra), in view of Lewis (supra) as applied to claim 1 above, and further in view of Sliwkowski (Sliwkowski, M.X. et al., J. Biol.Chem. 269: 14661-14665, 1994; IDS) or Carter (supra) was made to address one embodiment of the claimed methods where one maytansinoid conjugate was administered in combination with a second anti-ErbB2 antibody. This embodiment was view as a claim to a method where a combination of therapeutic agents was used. One agent was the maytansinoid conjugate, where the therapeutic efficacy resided in the maytansinoid part of the conjugate, and the second agent was the second anti-ErbB2 antibody that presumably effects a growth inhibitory or cytotoxic effect on the tumor cell. The claimed methods recite a step of determining that the tumor does not respond or responds poorly to treatment with an anti-ErbB2 antibody. The claimed methods do not indicate a specific anti-ErbB2 antibody. Therefore, the

tumor could fail to respond to the anti-ErbB2 antibody that is part of the conjugate but still respond to the other anti-ErbB2 antibody, because, for example, it happens to induce apoptosis, or it binds to a site on the receptor that inhibits ligand binding. Therefore, it is possible to construe the claims as drawn to methods using two different agents for the purpose of treating a tumor, and such a claim may be analyzed in light of In re Kerkhoven, because the court held that it is obvious to combine two compositions, in order to form a third composition, when each of the two compositions is taught by the prior art to be useful for the same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (MPEP 2144.06). In the instant case, the second anti-ErbB2 antibody may be the 2C4 antibody, which Sliwkowsky teaches inhibits the heterodimerization and signaling of ErbB2 receptors present on tumors, or may be the huMab4D5-8 of Carter that recruits immune effector cells to tumors. Since either of these antibodies may be used to treat tumors and the combination of Chari with Hudziak (supra), Baccus (supra), Huston (supra) or King (supra) teaches using maytansinoid conjugates to treat tumors, both the second antibody and the maytansinoid conjugate may be combined for the same purpose, treating a tumor.

16. Applicants arguments concerning the rejection maintained above in item #12 have been considered, but are not persuasive. Applicants argue that the cited references fail to provide any suggestion or motivation to combine, and also the cited references fail to provide a reasonable expectation of success. The motivation to combine the teachings of the references is derived from the teachings of Iwassa that maytansinoids may be targeted to a tumor using a bispecific antibody that contains one binding site that binds to a maytansinoid and a second site that binds

to a tumor antigen. Each of Carter, Huziak, Baccus, Huston, or King teaches antibodies that bind to a tumor antigen, ErbB2, and teaches that these antibodies are useful in methods of targeting toxins to tumor cells. Because each of Carter, Huziak, Baccus, Huston, or King teaches the use of their anti-ErbB2 antibodies as antibodies that would act as carriers to selectively deliver a toxin to tumor cells, the motivation to combine the references is that Iwassa teaches the desirability of increasing the selectivity of maytansinoid constructs and any of Carter, Huziak, Baccus, Huston, or King teaches that anti-ErbB2 antibodies are useful as carriers to increase the selectivity of toxins. For example, applicant has failed to show that there is any teaching in the prior art indicating that ErbB2 was not thought be a suitable antigen to target in tumor cells, or that prior to filing of the instant application, that the prior art failed to teach that ErbB2 was a known tumor antigen.

Applicant has also argued that one of ordinary skill in the art would not have had a reasonable expectation of success in treating a tumor with an anti-ErbB2 antibody-maytansinoid conjugate, where the tumor is one that does not respond, or responds poorly to treatment with an anti-ErbB2 antibody. Again, it is noted that the claims are not limited to methods comprising administering a maytansinoid conjugate to a mammal having a tumor that does not respond, or responds poorly to an anti-ErbB2 antibody. However, even if the claims were amended to change the scope of the administration step, methods for treating patients having tumors that do not respond or respond poorly to treatment with an anti-ErbB2 antibody would be obvious over the prior art, because tumors that do not respond to anti-ErbB2 antibodies are known to exist (teachings of Lewis) and because the growth inhibitory properties of the carrier antibody do not

appear to be relevant in a method comprising the use of a maytansinoid conjugate where the cytotoxicity of the maytansinoid conjugate is used to treat the tumor.

Double Patenting

17. The rejection o fclaims 1, 2, 4, 5, 8-12, 14-17, 20-33, and 38-41 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-18 of U.S. Patent No. 5,208,020 in view of in view of Hudziak (U.S. Patent 5,725,856; issued Mar. 10, 1998; effective filing date Jan. 12, 1988) and further in view of Lewis (Lewis, G.D. et al, Cancer Immunol. Immunother. 37: 255-263, 1993; cited in the IDS) is maintained for the reasons of record. Applicants have provided no arguments to consider.

The claimed methods are an obvious species of the claims 13-18 of U.S. Patent No. 5,208,020 in view the teachings of Lewis, that some tumors respond poorly to unconjugated anti-ErbB2 antibodies when other tumors respond well to the same antibodies despite overexpression of ErbB2, and in view of the fact that Hudziak clearly contemplated the use of anti-ErbB2 antibody-based immunotoxins in methods of treatment. A maytansinoid conjugated to an anti-ErbB2 antibody falls within the scope of an anti-ErbB2 immunotoxin of Hudziak. One would have been motivated to use the antibodies of Hudziak to make the maytansinoid conjugates to the claimed methods because Hudziak teaches that ErbB2 (Her-2) is amplified or overexpressed in many human malignancies (col. 2, lines 38-54) and because Lewis teaches that not all ErbB2 overexpressing tumors respond to unconjugated anti-ErbB2 antibodies.

New Grounds of Rejection:

18. Claims 1, 4-6, 8-21, 24-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1 has been amended to include a step of determining in a recognized in vitro model, animal model or human clinical trial that a tumor does not respond, or responds poorly, to treatment with an anti-ErbB2 antibody. Applicants point to page 25 as part of the specification that provides, in part, the support for this amendment. At page 25, lines 11-15, the specification defines a tumor that "does not respond, or responds poorly, to treatment with a monoclonal anti-ErbB antibody" as a tumor that does not show statistically significant improvement in response to anti-ErbB antibody treatment when compared to no treatment or treatment with placebo in a recognized animal model or a human clinical trial, or which responds to initial treatment with anti-ErbB antibodies but grows as treatment is continued. Although the other passages of the specification pointed to by applicant make mention of various in vitro cell models that may be used for testing the growth inhibitory properties of antibodies, these teachings do not appear to be directed to a definition for a tumor that "does not respond, or responds poorly, to treatment with a monoclonal anti-ErbB antibody" and do not appear to be directed to how to perform the step of determining whether a tumor does not respond or responds poorly to treatment with an anti-ErbB2 antibody. Therefore, claim 1 contains new matter in the recitation of step b, where the determination is made in a recognized in vitro model, animal model or human clinical trial.

Support is only found where determination is made in a recognized animal model or human clinical trial.

19. Claims 14-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendment to claim 14 adds the limitation that the antibody used in the claimed methods is one that shows a growth inhibitory effect on ErbB2 overexpressing cells selected from the group of cells consisting of SK-BR-3, BT474, Calu 3, MDA-MB-453, MDA-MB-361 and SKOV3 cells. Applicant points to page 6 and page 22 for support of this limitation. However, no support for this limitation is found. At page 6, line 17, there is a discussion of anti-ErbB2 cells that bind to essentially the same epitope as does Mab 4D5. At page 22, there is a discussion of how to screen for antibodies that induce apoptosis. As currently amended, the methods of claims 14-19 require the use of an antibody that has a biological characteristic of a 4D5 monoclonal antibody (ATCC CRL 10463) such that the antibody shows a growth inhibitory effect on ErbB2 overexpressing cells selected from the group of cells consisting of SK-BR-3, BT474, Calu 3, MDA-MB-453, MDA-MB-361 and SKOV3 cells. The specification only appears to teach screening for growth inhibitory antibodies with SK-BR-3 cells, and the specification does not appear to teach the 4D5 monoclonal antibody (ATCC CRL 10463) is growth inhibitory for SK-BR-3, BT474, Calu 3, MDA-MB-453, MDA-MB-361 and SKOV3

cells. Therefore, the amendment to claim 14 appears to introduce new matter into the specification and it does not appear that applicant was in possession of the claimed invention at the time the application was filed.

20. The amendment to the specification, filed June 18, 2004, is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment to page 55, adding the specific portions of U.S. Patent 5,208,020 that teach examples of maytansinoid conjugates and also the sentence "For example, for a compound as illustrated in Figure 3, "R" may be SH or may be SSR_1, where R_1 represents methyl, linear alkyl, branched alkyl, cyclic alkyl, simple or substituted aryl or heterocyclic." This amendment adds new matter to the specification because 1.) the amendment points to a specific passage in U.S. 5,208,020, which passage was not specifically pointed to at the time of filing, and 2.) the amendment adds an exemplification of the "R" group of Figure 3 (R may be SH or may SSR_1) that was not disclosed at the time of filing (only the exemplification that "R" may be SH in Figure 3 was disclosed at time of filing). The amendment introduces new matter because, although, U.S. Patent 5,208,020, is incorporated by reference, at the time of filing, the disclosure of the specification failed to identify specific portions of U.S. Patent 5,208,020 that were relevant. Amendment after filing to point out these specific portions or to exemplify the "R" group of Figure 3 amounts to redefining the scope of the "R" group of Figure 3. Changing the scope of the "R" group of Figure 3 adds new matter to the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran
Patent Examiner
September 10, 2004

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
9/14/2004